Doc Code: AP.PRE.REQ

PTO/SB/33 (01-09)
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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
133171.02501

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on _____

Signature _____

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Application Number	Filed
09719067	August 16, 2001
First Named Inventor	
David B. Weiner	
Art Unit	**Examiner**
1633	Robert M. Kelly

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [✓] attorney or agent of record. Registration number 52201
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

/Daniel M. Scolnick, Reg. No. 52,201/
Signature

Daniel M. Scolnick
Typed or printed name

610-640-7820
Telephone number

June 24, 2009
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of _____ forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: David B. Weiner *et al.*
Serial No.: 09/719,067
Filed: August 16, 2001

Group Art Unit: 1633
Examiner: Robert M. Kelly
Confirmation No.: 4038

Title: METHODS AND COMPOSITIONS FOR DELIVERING PROTEINS TO MACROPHAGE CELLS AND CELLS OF MACROPHAGE DERIVED LINEAGE

Mail Stop: AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Pre-Appeal Brief Request for Review

Dear Sir:

In response to the Final Rejection dated December 24, 2008, Applicants respectfully request reconsideration of the pending rejections.

I. Claims 9, 15, 16, 40-46, and 48 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for not having proper antecedent basis.

Applicants, solely in order to further prosecution, amended the claims in a response filed June 23, 2009. In view of the amendment, the Office has clearly erred because the terms in claims 9, 15, 16, 40-46, and 48 have sufficient antecedent basis. One of skill in the art would clearly understand what is being referred to and each phrases is supported by proper antecedent basis. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

II. Claims 9, 15, 16, 40-46, and 48 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent Publication No. 2004/0063652, Kataoka *et al*, (J. Biol. Chem., 272 (29):18209-15 (1997)), U.S. Patent No. 5,783,567, Samlowski *et al* ((1988) Regional Immunology, 1(1):41-55, and U.S. Patent No. 5,763,416.

The office has clearly erred by not properly establishing a *prima facie* case of obviousness and because U.S. Patent No. 5,783,567 teaches away from the present invention.

The Office has not established a *prima facie* case of obviousness, because the cited art has not been interpreted accurately by the Office. Moreover, there is nothing within the amorphous "combined knowledge" that would have led to the combination of the claimed invention. Finally, those skilled in the art viewing the art would not have recognized the benefits achieved by the claimed invention.

The pending claims are not obvious because the cited references do not yield the present invention, teach away from the pending claims, and even if the references are combined to yield the present invention do not give rise to a reasonable expectation of success. Claim 9 has previously been amended to recite the route of administration is intramuscular. Claim 40 has previously been amended to recite that the DNA molecule is a free DNA molecule. Free DNA molecule is referred to in Example 1 of the present application. Example 1 refers to the injection of a composition comprising bupivacaine and DNA and reflects that the DNA is not incorporated into particles or viral vectors.

None of the references discuss the step of identifying a lymphnode as a target for delivery of a protein and locating a site that is proximal to the lymphnode. None of the references disclose that upon administration of the DNA to an individual, the DNA is taken up by the macrophage cell and the macrophage then drains to the lymphnode.

The Jolly references discloses expressing a protein in a macrophage by introducing a vector that comprises the protein's nucleic acid coding sequence under the control of a macrophage specific promoter into a macrophage. Jolly, however, does not disclose how to administer the vector to the macrophage. Additionally, the Jolly reference fails to disclose the step of identifying a lymph node and the delivery of a protein to the lymph node by administering DNA to a site located on the individual's body that is proximal to the lymphnode.

The remaining references to do not make up the deficiencies of Jolly.

The Hedley reference teaches away from the use of free DNA and intramuscular administration. The Hedley references discusses microparticles that are effective for delivering DNA to be taken up by phagocytic cells. With reference to macrophages, the Hedley reference expressly teaches away from using intramuscular injection.

The Hedley reference discloses a specific method for delivering DNA that is encapsulated in microparticles to cells in the lymph node, stating: "one can target, via ***subcutaneous injection***, take up by the phagocytic cells of the draining lymph nodes." (Col. 8, lines 22-24, emphasis added). A careful reading of the Hedley reference reveals that the microparticles comprising DNA are injected subcutaneously and are taken up by cells in the lymph nodes. The Hedley reference teaches intramuscular administration of microparticles comprising DNA to target dendritic cells in the skin. *Id.* The Hedley reference does not teach intramuscular administration for delivery to macrophage cells which migrate to the lymph node. Rather, one skilled in the art reading the Hedley reference would conclude that subcutaneous delivery of microparticles is required to deliver the DNA to macrophage in the lymph nodes.

In addition to teaching away from using intramuscular injection, the Hedley reference also teaches away from using free DNA. The Hedley reference in its examples emphasizes the effectiveness of using microparticles to deliver DNA and how it is superior to using other forms of DNA including naked DNA. The Hedley references teaches one of skill in the art to use microparticles to deliver a DNA molecule instead of using naked DNA (see, for example, Hedley, Col. 18, lines 35-49). One of skill in the art, considering the Hedley reference in its entirety, would use microparticles as opposed to free DNA because the Hedley reference teaches the relative ineffectiveness of using free DNA.

One skilled in the art would not combine the Hedley reference with the combination of Jolly; Kataoaka et al, Samlowski et al and Bonadio et al. As noted above, Jolly does not disclose elements of the claims and the combination of Kataoaka et al, Samlowski et al and Bonadio et al. do not make up for the deficiencies in Jolly. Thus, there is no prima facie case of obviousness.

In addition, if one skilled in the art combined the teachings of Hedley with Jolly, Kataoaka et al, Samlowski et al and Bonadio et al., the benefits of the invention would not be expected. One of skill in the art would not have expected that intramuscular injection would result in delivery a protein to a lymph node nor would they expect that free DNA could be used to deliver a protein to a lymph node. None of the references cited indicate that intramuscular

injection of DNA would result in the delivery of DNA to macrophage which would then migrate to the lymph nodes. The combination of references simply does not provide any indication that such a result would be expected.

Likewise, the combination of references does not provide any indication that free DNA could be used to deliver DNA to macrophage which then migrate to the lymph nodes. The present specification states, "surprisingly the [free] DNA is not degraded in this process." (Specification, page 39, lines 5-6). There is nothing in the combination in the references that would have provided a reasonable expectation of success even if the combination had been made. As discussed above, the Jolly reference only refers to delivering a DNA molecule to a macrophage but does not teach how to do this. The Hedley reference specifies delivering DNA by using microparticles and that delivery of the microparticles to cells in the lymph nodes is achieved via subcutaneous injection. The other art cited by the Office does not give rise to an expectation of success for one of skill in the art. Therefore, based upon the cited prior art it there would not have been a reasonable expectation of success.

Prior to the present invention it was not known or obvious that one could deliver a protein to a lymphnode by the method described in the pending claims. Here, applicants have shown that DNA injected intramuscularly is taken up by macrophage which then travel to the lymph node, whereupon the DNA is expressed to effectively deliver the protein to the lymph node. Applicants have shown that free DNA directly injected into an individual remains intact and functional such that when taken up by macrophage which travel to the lymph node, the DNA can be expressed to effectively deliver the protein to the lymph node. Those skilled in the art would not have expected these beneficial aspects in view of the combination of references.

The Office alleges that Applicants argue that a specific motivation is required to combine the references and that specific motivation is no longer required. (See Office Action, p. 5). Although, specific or identified motivation may not be required the law still requires that the Office articulate sufficient reasons to support the legal conclusion of obviousness. The supreme court stated, "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some ***articulated reasoning*** with some rational underpinning

to support the legal conclusion of obviousness." *KSR*, 127 S. Ct. 1727, 1741 (2007). The Office has not put forward any articulated reasoning with some rational underpinning to support its legal conclusion of obviousness. The Office's only claim is that there are references that discuss macrophage specific expression and that microparticles can be taken up by macrophages via subcutaneous injection . The Office, however, has failed to articulate a reason why one of skill in the art would have extrapolated any of these methods to those to derive what is now claimed. Therefore, the claims are nonobvious because the Office has failed to articulate a reason with some rational underpinning to support its legal conclusion of obviousness for the reasons stated above. In view of the foregoing, Applicants request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Office is invited to contact Applicants' undersigned representative at 610-640-7820 to resolve any remaining issues.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully Submitted,

/Daniel M. Scolnick, Reg. No. 52,201/
Daniel M. Scolnick, Ph.D.
Registration No. 52,201

Dated: **June 24, 2009**
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